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Attorney Docket:
920522-905379

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FROM: William M. Lee, Jr.

TO: Examiner: Maher Haddad
Art Unit: 1644
The United States Patent and Trademark Office

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Attached: Corrected Response To Restriction Requirement Of February 13, 2004

If you do not receive all pages, please contact William M. Lee, Jr. at (312) 214-4800 or his assistant, Jennifer Ramirez at (312) 214-4829.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE THE APPLICATION OF

Jacquemin et al.

SERIAL NO.: 10/030,522

FILED: May 20, 2002

FOR: Ligands for Use in Therapeutic
Compositions for the Treatment of
Hemostasis Disorders)
)
) Examiner: Maher Haddad
)
) Group Art Unit: 1644
)
) Customer number: 23644
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)I hereby certify that this correspondence is being transmitted to
the above - identified examiner at the United States Patent and
Trademark Office (703) 872-9306 on April 5, 2004
Name of person signing Jennifer J. Ramirez
Signature [Signature]**CORRECTED RESPONSE TO RESTRICTION
REQUIREMENT OF FEBRUARY 13, 2004**Honorable Director of Patents and Trademarks
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the examiner's restriction requirement of February 13, 2004, it is requested
that the application be amended as follows:

In the Claims**1. - 26. (Cancelled)**

27. (Previously presented) A cell line named KRIX 1 deposited with the Belgian Coordinated Collections of Micro-organisms, under accession number LMBP 5089CB.

28. (Currently amended) A monoclonal antibody being able to recognize an epitope located in the C1 domain of factor VIII and having the capacity of at least 65% and at most 98% inactivating factor VIII or a complex of two or more factors involving factor VIII when the said monoclonal antibody is in a physiological excess by binding to a site of the said factor or complex.

29. (Currently amended) A cell line producing a human monoclonal antibody being able to recognize an epitope located in the C1 domain of factor VIII and having the capacity of at least 65% and at most 98% inactivating factor VIII or a complex of two or more factors involving factor VIII when the said monoclonal antibody is in a physiological excess by binding to a site of the said factor or complex.

30. (Previously presented) A monoclonal antibody according to claim 28, wherein the binding site of the monoclonal antibody is not directly involved in a physiological interaction of the said factor or complex.

31. (cancelled)

32. (Previously presented) A monoclonal antibody according to claim 28, being produced by on purpose immunization in animals.

33. (Previously presented) A monoclonal antibody according to claim 28, being produced by on purpose immunization in animals and being humanized.

34. (Currently amended) An antigen-binding fragment Fab, Fab' or F(ab')₂, a complementarity determining region, a soluble or membrane-anchored single-chain variable part, a single variable domain or a derivative of a monoclonal antibody being able to recognize an epitope located in the C1 domain of factor VIII and having the capacity of at least 65% and at most 98% inactivating factor VIII or a complex of two or more factors involving factor VIII when the said monoclonal antibody is in a physiological excess by binding to a site of the said factor or complex.
35. (Currently amended) A pharmaceutical composition for the prevention or treatment of disorders of hemostasis and resulting pathologic conditions in mammals, comprising as an active ingredient a monoclonal antibody being able to recognize an epitope located in the C1 domain of factor VIII and having the capacity of at least 65% and at most 98% inactivating factor VIII or a complex of two or more factors involving factor VIII when the said monoclonal antibody is in a physiological excess by binding to a site of the said factor or complex, or a fragment, derivative or homolog thereof, in admixture with a pharmaceutically acceptable carrier.
36. (Previously presented) A pharmaceutical composition according to claim 35, further comprising a therapeutically effective amount of a thrombolytic agent.
37. (cancelled)
38. (Previously presented) A method of obtaining monoclonal antibodies from a non-human mammal, comprising the steps of:
- a) selecting a non-human mammal having a modified and partially functional protein, the modification being with respect to a wild type protein and lying in a domain of the protein;
 - b) administering the wild type protein to the non-human mammal in order to elicit an immune response, and

c) selecting B-lymphocytes from the non-human mammal which produce antibodies which only partially inactivate the wild type protein.

39. (Previously presented) A method of obtaining monoclonal antibodies from the blood of a human being having a modified and partially functional protein, the modification being with respect to a wild type protein and lying in a domain of the protein, and to whom the wild type protein was administered, the said method comprising the step of selecting, from the blood of said human being, B-lymphocytes which produce antibodies which only partially inactivate the wild type protein.
40. (Previously presented) A method according to claim 39, wherein the wild type protein is a factor or a complex of two or more factors involved in the coagulation cascade of blood.
41. (Previously presented) A method according to claim 39, wherein the wild type protein is factor VIII or a complex including factor VIII.
42. (Previously presented) A method according to claim 39, wherein the wild type protein is a protein involved in a proteolytic cascade.
43. (Previously presented) A method according to claim 39, wherein the wild type protein is a complement factor.
44. (Withdrawn) method of treatment and/or prevention of a disorder of hemostasis, coagulation disorder or thrombotic pathologic condition or attenuation of coagulation in a mammal, comprising administering to a mammal in need of such treatment or prevention or attenuation of coagulation a therapeutically effective amount of an active ingredient selected from a monoclonal antibody able to recognize an epitope located in the C1 domain of factor VIII and having the capacity of at least 65% and at most 98% inactivating factor VIII or a complex of two or more factors involving factor VIII when the said monoclonal antibody is in a

physiological excess by binding to a site of the said factor or complex or a fragment, derivative or homolog thereof.

45. (Withdrawn) A method according to claim 44, wherein the thrombotic pathologic condition is selected from intravascular coagulation, arterial thrombosis, arterial restenosis, venous thrombosis and arteriosclerosis.
46. (Withdrawn) A method according to claim 44, wherein the active ingredient is provided to the mammal by oral, intranasal, subcutaneous, intramuscular, intradermal, intravenous, intraarterial or parenteral administration or by catheterization.
47. (Withdrawn) A method according to claim 44, further comprising administering to the mammal, simultaneously or sequentially with the said active ingredient, a therapeutically effective amount of a thrombolytic agent.
48. (Cancelled)

Response

In response to the restriction requirement, the applicants have elected Group I, and do so with traverse, for the reasons discussed below.

In the comments in numbered section 5 at the top of page 3 of the office action (not numbered section 5 at the bottom thereof), the examiner makes certain comments concerning the antibodies of the prior art and the burden of proof falling on the applicants. There is insufficient time to respond further in the one month allotted, and the applicants reserve any further comments to when the examiner issues a substantive office action.

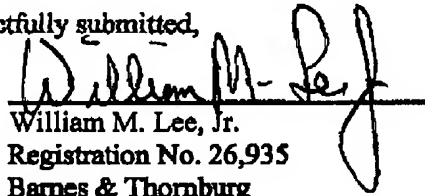
In electing Group I, and to avoid any question of applicability of the reference cited by the examiner, the claims have been amended to direct them to the feature of former claim 31, which has now been cancelled. There is no prior art relating to antibodies directed to an epitope of the C1 domain of factor VIII which have the capacity of at least 65% and at most 95% interactivating factor VIII.

The examiner had considered method claims 38 through 43 as part of the invention of Group I, but has required restriction in relation to claims 44 through 47, which have been identified above as "withdrawn". Claim 44 has been amended in the same manner as the other independent claims, and it is therefore submitted that claims 44 through 47 should also, therefore, now be considered to be part of Group I.

Reconsideration and further action on the application are therefore awaited.

April 5, 2004

Respectfully submitted,

A handwritten signature in black ink, appearing to read "William M. Lee, Jr.", is written over a horizontal line.

William M. Lee, Jr.

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